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Original research article

A study on role of platelet indices - platelet large cell ratio (P- LCR), mean platelet volume [MPV], platelet distribution width [PDW] and high-sensitivity C- reactive protein (hs CRP) as predictive markers for complications in Type 2 diabetes mellitus

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Abstract

Background and Aims: A "prothrombotic propensity" with enhanced platelet reactivity has been identified in diabetes mellitus (DM). According to theories, the microvascular consequences of diabetes may be influenced by this increased responsiveness. Mean platelet volume (MPV), one of the platelet indices, shows changes in either platelet stimulation or the rate of platelet synthesis. A measurement of platelet heterogeneity is platelet distribution width (PDW), which can be brought on by either the ageing of platelets or the uneven demarcation of megakaryocytes. Platelet-large cell ratio (P-LCR), the third platelet index, is a measurement of bigger platelets. A small number of research on diabetic people have examined MPV. Diabetes, metabolic syndrome, and stroke have all been linked to an increase in MPV.

Early detection of the occurrence of such complications would aid in lowering these unfavourable outcomes because microvascular complications of DM are significant sources of morbidity and health care expenditures.

High-sensitivity C - reactive protein (hs CRP), according to studies, is a significant risk factor for cardiovascular disease. In order to determine if platelet indices and high-sensitivity C-reactive protein (hs-CRP) levels may be utilised as predictors of glycemic control and vascular problems, this study was conducted.

Materials and Methods: In all, 50 diabetes patients and 100 non-diabetic individuals (the control group) participated in this study. Parameters of HbA1c ≥ 6.5 or postprandial plasma glucose (2 h) levels >200 mg/dL or fasting blood glucose ≥ 126 mg/dL were taken into consideration.

On the basis of clinical presentation, investigation, and examination, the diabetic group was further classified into diabetics without (60) and with complications (40). Using a complete blood count analyzer, platelet indices (mean platelet volume [MPV], platelet distribution width [PDW], and platelet large cell ratio [P-LCR]) were evaluated. Hs-CRP testing was qualitative, and those samples that proved positive underwent quantitative evaluation.

Observation: When compared to the non-diabetic group, all three of the examined platelet indices - MPV, PDW, and P-LCR - were considerably greater in diabetics. They also rose with rising HbA1c levels. Only P-LCR, when linked with HbA1c, however, demonstrated a significant difference between diabetics with and without problems (P = 0.002), while MPV shown a significant difference across all categories (P 0.04). The difference in hs-CRP concentrations between diabetics with and without problems was statistically significant (P = 0.01)

Conclusion: Continuously rising MPV, PDW, and P-LCR values with declining glycemic control demonstrate chronic creation of bigger platelets with increased activity in diabetics due to continued inflammation. Since the sole parameter in our study that demonstrated a significant difference between diabetics with and without difficulties, P-LCR should be the preferred index for predicting the likelihood of future complications.

Keywords: Platelet indices, thromboses, inflammation, hba1c, diabetes

Introduction

A developing pandemic metabolic condition known as diabetes mellitus (DM) affects almost 5.6% of people worldwide. This illness accounts for over 12% of healthcare expenditure. Because to the long-

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lasting silent clinical presentation of DM, finding and creating biomarkers as a practical guideline with high specificity and sensitivity for the diagnosis, prognosis, and clinical management of DM is one of the issues of significant interest among DM researchers. Type 2 diabetes mellitus (T2DM) is an endocrine condition marked by the body's tissues exhibiting insulin resistance and poor pancreatic insulin excretion. DM is characterized by varying degree of hyperglycemia accompanied with the biochemical alterations in carbohydrate, protein, and lipid metabolism. Deaths due to diabetes are increasing and there is a need to prevent these deaths by early diagnosis of impending complications.

Patients with T2DM who have chronic hyperglycemia have micro- and macrovascular problems. A number of variables may contribute to the development of complications, including the length of diabetes, dyslipidemia, hereditary factors, obesity, hypertension, smoking, proteinuria, and hypermetropic refractive alterations. In T2DM patients, abnormal insulin activation may enhance platelet activation and hasten microvascular problems. The role of platelet dysfunction in macrovascular (CVD, stroke, and peripheral artery disease [PAD]) and microvascular (nephropathy, neuropathy, and retinopathy) complications, which increase morbidity and mortality in T2DM, has been highlighted by some authors.

When compared to non-diabetics, patients with Type 2 DM have a 2-4-fold higher risk of developing preventable vascular angiopathies, including macrovascular conditions like coronary artery disease, peripheral arterial disease, and stroke, as well as microvascular conditions like diabetic neuropathy, nephropathy, and retinopathy. Thus, risk factor changes and treatments are required to lessen the effects of such problems [1, 2, 3].

Mean platelet volume (MPV), a marker for platelet function, is crucial for maintaining the integrity of normal homeostasis. The bigger platelets are more thrombogenic and potent than the smaller platelets because they have more packed granules, synthesise more thromboxane A2, platelet factor A, and beta-thromboglobulin, and have more of these factors in common. The size and quantity of granules in blood platelets are independently regulated by hormones and remain constant over the course of a platelet's lifetime [4, 5, 6, 7].

These vascular problems are related to altered platelet shape and functions that have been seen in diabetes individuals. The development and maintenance of vascular problems are believed to be significantly influenced by the enhanced reactivity and baseline activation of platelets from type 2 diabetes mellitus patients. A set of connected changes brought on by persistent hyperglycemia can clearly show endothelial dysfunction and result in vascular problems. Furthermore, P2Y12 signalling and hyperglycemia-induced up-regulation of glycoproteins (Ib and IIb/IIIa) are important processes driving atherothrombotic risk in T1DM and T2DM. The probable processes by which elevated glucose promotes vascular abnormalities include the formation of advanced glycation end products, activation of protein kinase C, and disruptions in polyol pathways [8, 9].

A daily automated blood count includes parameters for measuring platelet indices (PI), indications of platelet activity. PI are connected to the shape and kinetics of platelet growth. The mean platelet volume (MPV), platelet distribution width (PDW), platelet-large cell ratio (P-LCR), and plateletcrit are the PI parameters that are most frequently evaluated (PCT) [10]. Due to their relatively easy accessibility and affordable methods of assessment, blood-based platelet parameters appear to be on the increase as possible new biomarkers of many illnesses, both acute and chronic [11]. Platelet count, plateletcrit, and mean platelet indices (MPI) are a few indicators that represent the state of platelets (mean platelet volume [MPV], platelet distribution width [PDW], and platelet large cell ratio [PLCR]). Race, age, smoking, drinking, and physical activity are just a few of the many variables that might affect MPV. As a possible indicator of a patient's prognosis, MPV has been studied, and most studies link a greater number to a poorer clinical result. Regardless of the adjusted level of other well-known prognostic indicators, a research by Lembeck *et al*. demonstrated a substantial correlation between high MPV and a poorer prognosis in individuals with pancreatic ductal adenocarcinoma. This was also seen in myocardial infarction patients, where individuals with greater MPV levels appeared to have worse clinical outcomes more frequently. Low-grade inflammation, such as rheumatoid arthritis, is linked to lower MPV levels [12].

The MPV represents the typical platelet size. It is a measure for subclinical platelet activation and may become more pronounced in certain vascular disorders such myocardial infarction (MI), coronary artery disease (CAD), cerebral ischemia, and PAD. Additional platelet indicators, which represent platelet shape and are useful in vascular events like atherosclerosis and thrombosis, include PDW, PLCR, and plateletcrit (PCT).

PDW provides information on platelet size distribution, PLCR provides information on the proportion of younger platelet groups with the highest volume, and PCT provides information on the overall mass of platelets.

The size distribution of platelets generated by megakaryocytes is described by the platelet distribution width (PDW), which rises in response to platelet activity. There is little to no evidence for the vast range of variance stated in the literature, despite Budak *et al*. suggestion’s review's that PDW reference values range between 8.3 and 56.6%. Studies that were examined revealed that this parameter varied between

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10% and 18% in healthy people and that PDW changed in patients with a variety of disorders [13, 14].
It enables this characteristic to be taken into consideration as a possible biomarker. In healthy persons, PDW and MPV appear to be proportionately correlated; yet, in non-physiological circumstances, such as threatened preterm labour, they exhibit considerable dissonance, with PDW rising and MPV falling. When Aydogan *et al*. analysed MPV and PDW levels in patient groups with perforated and non-perforated acute appendicitis, they discovered the same discrepancy. According to Amin *et al*., megakarycote hyperplasia can be caused by people with sickle cell disease having greater levels of PDW during vaso-occlusive crises [17].
Another indicator of platelet activity is the platelet larger cell ratio (P-LCR), which is calculated as a proportion of all platelets having a bloodstream circulation volume greater than 12 fL. Typically, it lies between 15% to 35% [18].
Total platelet mass is quantified by plateletcrit (PCT), which expresses it as a percentage of blood volume occupied. PCT typically falls between 0.22% and 0.24%. It appears to be a useful screening tool for identifying quantitative platelet abnormalities. The PCT and platelet count have a nonlinear correlation that suggests a similar clinical impact. Patients with low high sensitivity C-reactive protein were studied for PCT's potential as a new biomarker of active Crohn's disease by Tang *et al*. (hs-CRP) [19, 20].
The use of platelet indices as possible new biomarkers for diagnosis and prognosis in a variety of acute and chronic disorders is now being thoroughly investigated. PI are readily available and affordable to measure during normal blood counts.
Research on the association between diabetes complications and MPV, PDW, and PCT values - values that reveal changes in platelet shape and function - have been reported.
To our knowledge, however, this is the first study examining all of the morphologic indicators (MPV, PDW, PLCR, PCT, and platelet count) between phases of complications from diabetes [21, 22].
It is straightforward, quick, and affordable to identify individuals with aberrant platelets during regular haematological analysis, which can serve as a useful signal for prompt intervention and avoidance of the consequences indicated above [23, 24, 25, 26].

Platelet Indices (PI)	Normal range	Conditions with platelet indices above normal range	Conditions with platelet indices below normal range
MPV	7.2-11.7 fL	Immune thrombocytopenia purpura (ITP) Diabetes mellitus DM related retinopathy and nephropathy Heart disease Malignant tumors Complicated acute appendicitis	Non-complicated acute appendicitis acute cholecystitis Low-grade inflammation ex. rheumatoid arthritis Threatened preterm labor
PDW	8.3-56.6%	DM related retinopathy and nephropathy ST-elevation myocardial infarction acute cholecystitis threatened preterm labor vaso-occlusive crisis sickle cell disease	Non- malignant tumors
P-LCR	15-35%	Immune thrombocytopenia purpura (ITP) DM related retinopathy and nephropathy	Myeloid insufficiency
PCT	0.22-0.24%	Acute cholecystitis. Active Crohn’s Disease with low hs-CRP	Immune thrombocytopenia purpura (ITP)

Highly sensitive C-reactive protein (hs-CRP), an acute phase protein secreted by the liver and other tissues in response to any inflammatory condition, has been identified as one of the most significant pro-atherosclerotic mediators in recent years and is now routinely used to predict the development of cardiac complications in both non-diabetics and type 2 DM patients. In order to associate platelet indices and hs-CRP levels with glycemic control and vascular problems, this study was carried out with the hope that, if significant, they may be added to the variables affecting diabetes patients' prognosis and outcomes.

Table 1: Comparison of Mean (SD) value parameters in the various study groups

	Groups A= Controls B= Diabetics without complication C= Diabetics with complication		
Parameter	**Controls (A) (n=50)**	**Diabetics without complication (B) (n=60)**	**Diabetics with complication (C) (n=40)**
HbA1c	5.2 (0.38)	8.8 (2.44)	9.4 (2.6)
MPV	9.6 (1.12)	10.22 (1.4)	10.4 (1.6)
PDW	13.2 (1.60)	15.2 (2.10)	14.8 (2.30)
L-PCR	28.33 (7.10)	30.2 (9.2)	34.2 (6.8)

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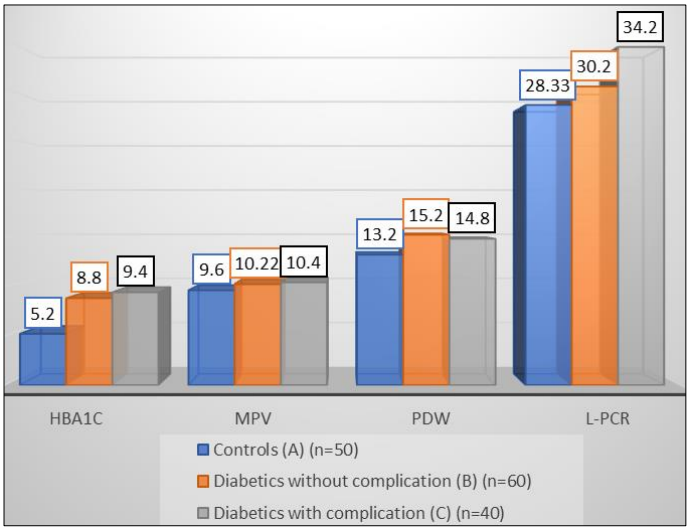

Fig 1: Mean values of the various parameters in the study groups.

Table 2: Comparison of P value of the parameters in the various study groups

	P value comparison in various groups		
Parameter	**P value in (Controls VS Diabetics without complications)**	**P value in [Controls VS Diabetics with complications]**	**P value in Diabetics without complications VS Diabetics with complications**
HbA1c	0.0001 [S]	0.0001 [S]	[NS]
MPV	0.03 [S]	0.003 [S]	[NS]
PDW	0.0001 [S]	0.0001 [S]	[NS]
L-PCR	0.04 [S]	0.0001 [S]	0.002 [S]
P value	[S]: Significant, [NS]: Not significant, MPV: Mean platelet volume, PDW: Platelet distribution width, PLCR: Platelet large cell ratio		

Table 3: Comparison of Mean (SD) value of the Platelet parameters with Glycemic control (HbA1C) in the various study groups

Parameter	HbA1C (≤7%) (A)	HbA1C (7.1–8%) (B)	HbA1c (>8%) (C)
MPV	9.71 (1.23)	10.31 (1.32)	10.82 (1.04)
PDW	14.2 (2.35)	14.32 (2.1)	14.52 (2.1)
L-PCR	30.49 (7.65)	31.25 (7.48)	32.21 (7.61)

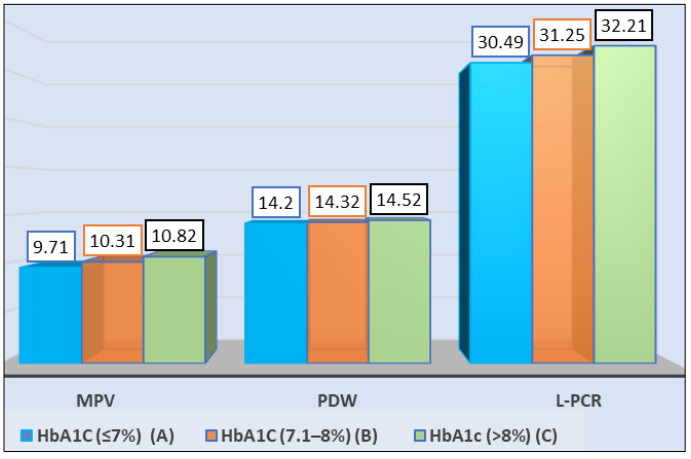

Fig 2: Mean values of the various parameters in the HbA1C groups

Table 4: Comparison of P value of the Platelet parameters with Glycemic control (HbA1C) in the various study groups

Parameter	P value in [HbA1C (≤7%) VS HbA1C (7.1–8%)]	P value in [HbA1C (≤7%) VS HbA1c (>8%)]	P value in [HbA1C (7.1–8%) VS HbA1c (>8%)]
MPV	0.047 [S]	0.0001 [S]	0.04 [S]
PDW	[NS]	[NS]	[NS]
L-PCR	[NS]	[NS]	[NS]
P value	[S]: Significant, [NS]: Not significant, MPV: Mean platelet volume, PDW: Platelet distribution width, PLCR: Platelet large cell ratio		

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Table 5: Comparison of Mean (SD) value of hs CRP in the various study groups

Parameter	Controls (A) (n=50)	Diabetics without complication (B) (n=60)	Diabetics with complication (C) (n=40)
hs-CRP	19.99 (5.83)	29.6 (4.76)	55.28 (28.1)

Table 6: Comparison of P value of hs CRP in the various study groups

Parameter	P value in (Controls VS Diabetics without complications)	P value in [Controls VS Diabetics with complications]	P value in Diabetics without complications VS Diabetics with complications
hs-CRP	[NS]	0.03 [S]	0.01 [S]

Materials and Methods

Patient population and study design

Along with the department of medicine, the pathology department carried out the study. The regional ethics committee gave the study its approval.

Each participant gave their informed permission before being included in the research. 100 diabetes patients and 50 control participants were included in this study. Based on clinical presentation, research, and examination, the diabetic group was further split into diabetics without issues (60) and diabetics with complications (40).

Statistics

The data were entered into an Excel Sheet master chart, where various metrics in separate groups were compared. Student's unpaired "t" test and the chi-square test, with or without Yates' adjustment, were applied when and where necessary. The crucial level of statistical significance was set at P 0.05.

Results

In all, 50 controls (group A), who were matched for age and gender, and 100 diabetes patients were included in the research. On the basis of clinical information and examination, the diabetic group was further split into diabetics with complications (group B) and diabetics without complications (group C).

I. Control (group A): This research contained 50 controls. The control group was selected using threshold values of HbA1C 5.7% and fasting blood glucose 100 mg/dl to ensure that even borderline diabetics were not included in the trial.

II. Diabetics (group B & C): This study comprised 100 diabetes individuals.

For inclusion in this group, a value of HbA1C $\geq$ 6.5%, a fasting blood glucose level $\geq$ 126 mg/dl, or a postprandial blood glucose level $\geq$ 200 mg/dl was used as the cutoff.

Based on clinical information and other research, out of these 100, 60 (60%) had no linked issues (group B), while the remaining 40 (40%) experienced complications (group C). The three groups' HbA1c and platelet indices were assessed, compared, and their levels of significance were examined. PLCR value was significantly higher in diabetics along with a significant difference seen between diabetics with complications and without complications (P = 0.002). Whereas MPV and PDW were significantly higher in diabetics compared to Control group, they did not show any significant difference with regard to presence or absence of complications.

Platelet indices and their relation to HbA1c level: The diabetes individuals were divided into three groups based on the levels of glycosylated blood (HbA1c): mild (7%), moderate (7.1-8%), and severe (>8%). Across these groupings, many platelet properties were examined. Although while all three of the platelet indices - MPV, PDW, and P-LCR - increased with rising HbA1c levels, a statistically significant difference was only observed with MPV ($P \leq 0.04$) among all the subgroups.

hs-CRP

CRP was measured in all of the patients using the latex agglutination method, and 16 cases of positive results were found; these results were quantitatively evaluated using the turbidimetric method. Out of 19, 14 had problems from their diabetes, three did not, and two were in the control group. Averages (SD) for various groupings. For diabetics without and with complications, there was a significant difference in the values (P = 0.01).

Discussion

Chronic hyperglycemia is a key feature of the complicated metabolic syndrome known as DM, which also includes problems mostly brought on by micro- and macro-angiopathic alterations. A "prothrombotic condition" with increased platelet reactivity is what is being described. Chronic problems in diabetics are brought on by inadequate glucose management, protein glycation, and oxidative stress, which damage endothelial cells and activate platelets with altered form and function. Many studies have

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demonstrated that bigger platelets, which are more metabolically and enzymatically active and have a higher thrombotic capacity, play a role in the aetiology of vascular problems.
Enhanced platelet sensitivity is associated with improved content release from platelet granules, which in turn causes a platelet volume gradient, an increase in platelet turnover rate, and a decrease in platelet survival. Many platelet indices, including PC, PCT, MPV, PDW, and P-LCR, aid in determining platelet proliferating activity. The goal of the current study was to determine how diabetics' micro- and macrovascular problems related to their platelet indices (excluding PC and PCT) and hs-CRP levels, glycemic control, and glycemic control.

MPV

When compared to the non-diabetic Control group in our study, diabetics had MPV levels that were noticeably higher. Regarding the presence or lack of problems, there was, however, no discernible difference. Our results agreed with those from a few prior research. The MPV of diabetics with and without problems, however, varied significantly between studies, suggesting that continuous thrombosis causes larger, more recent platelets to be discharged into circulation, which raises MPV. A substantial number of big platelets, which are more recent, dense, and active, are present when MPV levels are high. Thus, the chance of vascular problems is increased by greater MPV readings. Previous investigations discovered high MPV to be related to CAD, OAD, and cerebral ischemia [27, 28, 29, 30].
According to Ates *et al*., there was no significant difference between individuals who had baseline retinopathy and those who developed retinopathy later; nevertheless, MPV values were considerably greater in patients with T2DM compared to controls [31]. Similar findings were observed by Citirik *et al*. [32] Aydinli *et al*., on the other hand, supported the idea that there was no connection between MPV and vascular problems in T2DM [33]. Our investigation revealed non-statistically significant greater MPV in diabetes patients with micro and macrovascular problems compared to non-diabetic controls, which is consistent with research by Kodiate *et al*. and Mowafy *et al*. [34, 35] Nevertheless, Papanas *et al*. and Demirtas *et al*. found that diabetics with problems had considerably greater MPV than diabetics without issues in their study. This suggested that elevated platelet activity had a role in the aetiology of vascular problems [36, 37].
We discovered a statistically significant difference in MPV levels between T2DM patients and HCs in the current investigation. When we contrasted the various diabetes patient populations. As a new independent risk factor for thromboembolism, stroke, and myocardial infarction, increased MPV is currently being identified [38].
Stroke and myocardial infarction occur more often in type 2 DM patients [39]. An noteworthy finding that raised the possibility of thrombotic consequences was the presence of elevated MPV in these individuals. Moreover, type 2 DM patients with retinopathy and other symptoms have been observed to have higher MPV levels than those without this issue.
Hekimsoy Z *et al*. did not find any correlation between MPV and FBG in patients with type 2 diabetes mellitus, we found a correlation between MPV and FBG [40]. Shimodaira *et al*. also confirm a relationship between MPV and FBG in prediabetic subjects. Our results are consisted with their study [41]. Kodiatte *et al*. reported that increased platelet activity have an important role in the development of vascular complications in type 2 DM [34].
It can be suggested that increased platelet volume may be an important factor in the enhanced risk of vascular complications in these cases. In this respect, MPV can be used as a favorable test in the monitoring of type 2 DM in terms of atherosclerosis development. According to Farah *et al*., RDW and MPV indicators rose together with the severity of Type 2 Diabetes and the Metabolic Syndrome. Patients with Metabolic Syndrome had higher levels of MPV, according to Abdel-Moneim *et al*. According to Zhao *et al*. research's MPV and Metabolic Syndrome in women are inversely associated. Moreover, gestational diabetes mellitus, congestive heart failure, and coronary artery ectasia have all been linked to increased MPV.
Kakouros N *et al*. suggested that hyperglycemia causes to generate of larger platelets [42]. Abnormal platelet-endothelial interactions have been identified as an essential pathogenic mechanism in the development of atherosclerosis [43]. Endothelial cell injury may have an impact on the aetiology of cardiovascular illnesses, according to some research. Hyperglycemia, more free fatty acids, different lipoproteins, hypertension, and type 2 DM can all cause endothelial cell injury. It is hypothesised that hyperglycemia can improve platelet reactivity by activating protein kinase C, the nonenzymatic glycation of platelet proteins, and the osmotic action of glucose.
Moreover, Schneider DJ *et al*. hypothesised that by boosting the synthesis of megakaryocytic glycoprotein, hyperglycemia would amplify platelet activity [44].

PDW

PDW indicates the heterogeneity in platelet morphology, varies with platelet activity, and directly evaluates platelet size variability. Similar to other investigations, the PDW value in the present study was considerably greater in diabetics than in controls. Yet, there was no discernible difference between

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diabetics with and without problems. Several earlier investigations, such those by T. Ishibashi *et al*., have demonstrated a substantial difference in PDW between these two groups [45]. The increased synthesis and activation of big platelets in diabetics leads to a high PDW score. PDW also enhances the variability of platelet volume distribution and is a particular measure of platelet activation. While stating that PDW is a more specific measure, Vagdatli *et al*. showed that MPV and PDW were enhanced jointly with platelet activation [46].

PDW was discovered to be an independent risk factor for cardiac mortality and for the incidence of either death, recurrent MI, or the requirement for another revascularization treatment in the study by Rechcnski *et al*. [47].

According to Jindal *et al*., PDW was considerably greater in T2DM patients and was even higher in those who experienced microvascular problems. [22] Although Citirik *et al*. discovered greater PDW levels in diabetic patients relative to healthy controls, this finding lacked statistical significance. In our study, T2DM patients' PDW levels were substantially greater than those of controls. Diabetes patient groups' PDW levels rose. Moreover, diabetic participants' other platelet indices (PDW) were likewise considerably greater than controls' ($p = 0.003$, respectively) in comparison to diabetes subjects. Similar findings with noticeably increased PDW levels among diabetes subjects were found in additional investigations conducted by Demirtas *et al*. [37] Jabeen *et al*., [48] and Dalamaga *et al*. [49].

PLCR

P-LCR, which measures the proportion of platelets in the total PC that have a volume greater than the typical value of 12 fL, is used to track platelet activity. In the current investigation, diabetics' P-LCR values were substantially greater than those of the control group. Moreover, a substantial distinction between diabetics with and without problems was seen. According to Shilpi *et al*. and Hong *et al*., this was the case.

Nevertheless, some researchers found no appreciable differences in the presence or lack of complications in their individual trials. P- LCR was higher in our sample, most likely as a result of a chronic microvascular phenomena that causes a compensatory production of activated platelets [50, 51]. Another measure for platelet volume is called PLCR, and it shows which platelet fraction is the greatest. The biggest platelet type, freshly generated platelets, frequently rise in quantity concurrently with an increase in PLCR. PLCR and MPV are often associated, although PLCR is more responsive to an increase in platelet size. Babu and Basu demonstrated that PLCR is directly connected to MPV and PDW and inversely correlated with platelet count [52]. This is consistent with research by Jindal *et al*. and Ashraf *et al*., [53] which found that those with diabetes had much greater P-LCR than people without the disease.

A rise in PLCR may signal the existence of large platelets, microerythrocytes, and platelet aggregates. After an acute MI, PLCR can be an effective prognostic indicator for long-term mortality in patients. According to Rechcnski *et al*., PDW and PLCR are predictive indicators after MI and may be superior to other markers, notably MPV. According to Malachowska *et al*., Type 1 DM patients had considerably higher PLCR [54]. In a prior study, Jindal *et al*. investigated the relationships between PLCR and T2DM microvascular complications and discovered that although diabetic patients in general and those with diabetes and microvascular complications in particular have higher PLCR values, the difference was not statistically significant. This marker needs to be the subject of more study. In our investigation, the diabetic groups' PLCR values were statistically substantially greater than those of the HC group. Although there was a correlation between PLCR levels and the severity of diabetic complications, this relationship was not statistically significant. In our study, diabetics with HbA1c levels of 6.5% had substantially greater MPV, PDW, and P-LCR values than diabetics with HbA1c levels of 6.5%. According to research by Kodiatte *et al*., Ozder and Eker, Ulutas *et al*., [56] and Demirtas *et al*., this is the case. The observation in the study by Kodiatte *et al*. was similar in that there were more diabetics with HbA1c values of 6.5% [9].

This may have occurred as a result of poor eating habits and ignorance of the diabetes-specific diet and exercise regimens that should be followed. Moreover, Ozder and Eker came to the conclusion that HbA1c and MPV tend to decline as glycemic control increases. Glycemic management therefore enhances platelet activity and function and may prevent potential diabetic vascular problems. Hepatocytes create the acute phase reactant known as hsCRP. It is a well-known general indicator of tissue injury and inflammation. The American Heart Association and the Centers for Disease Control and Prevention advised patient stratification into three groups in 2003 for determining cardiovascular disease risk:

Low risk (hs-CRP <1 mg/L), intermediate risk (hs-CRP 1–3 mg/L), and high risk (hs- CRP >3 g/L).

They also came to the conclusion that hs- CRP was the ideal analyte for locating individuals for cardiovascular disease primary prevention. Between diabetics with problems and controls, as well as the subgroup of diabetics without complications, the value of hs-CRP revealed a significant difference. This was consistent with a few prior findings that mentioned greater CRP values in the diabetes group with problems. The microvascular thrombosis brought on by the inflammatory process may be the origin of

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the elevated CRP reactivity seen in diabetics with complications. Also, we divided the diabetic patients into three categories based on the amount of glycosylation (HbA1c): mild (≤ 7%), moderate (7.1-8%), and severe (>8%).

Only with MPV did the platelet indices show a significant difference between all the groupings. Similar results have been reported by other authors, although according to Bhanukumar *et al*., despite the fact that MPV and PDW values are greater in diabetic individuals, they do not correlate with HbA1c levels. In the current investigation, we discovered that PDW and P-LCR levels were marginally higher in patients with moderately elevated HbA1c levels, and they further rose in patients with significantly elevated HbA1c levels, although they were not statistically significant.

Bhattacharjee *et al*. and Demirtas *et al*., however, claim that they dramatically alter in response to variations in HbA1c levels. Only diabetic individuals with modestly and significantly elevated HbA1c showed a change in hs-CRP levels.

In a quite similar study, Shi *et al*. divided diabetic patients, according to their HbA1c levels, into three groups: HbA1c ≤9.32%, HbA1c >9.32 and ≤11.76%, and HbA1c >11.76%. They discovered that all three groups had significantly varied levels of hs-CRP. HbA1c and hs-CRP were correlated in another investigation, and patients with hs-CRP 1 mg/dl had HbA1c values that were significantly different from those of patients with hs-CRP >1 mg/dl.

The current study found that patients' hs-CRP reactivity increased as HbA1c control declined, indicating that diabetics with poorly managed HbA1c levels had more widespread vascular thrombosis-related inflammation.

Although PC and PCT have been taken into account in a number of articles that have explored the function of platelet indices in predicting the development of problems in diabetics, we have not done so due to the significant variability that these two parameters exhibit with relation to a variety of environmental variables. Due to funding limitations, only those 16 instances in this study that had good results from qualitative assessment of the platelet indices and hs-CRP were given quantitative estimations. The current study supports the hypothesis that chronic microthrombi are formed in diabetics as a result of continuing inflammation, causing platelets to be consumed and larger, more active platelets to be produced.

A consistent rise in the value of platelet indices, particularly MPV, PDW, and P-LCR, together with deteriorating glycemic control, highlights how important it may be to regularly test these markers to identify diabetics who are more susceptible to experience vascular problems. Although hs-CRP is regarded as a very sensitive indicator of vasculopathy, further studies comparing it to specific platelet indices would enable us to see the situation more clearly. We also want to point out that, among the three variables MPV, PDW, and P-LCR, the latter one should be the one used to forecast the likelihood of a future problem because, in our study, it was the only one that significantly differentiated diabetics with complications from those without.

In individuals with type 2 DM, elevated MPV and PDW can be utilised as indicators of an imminent arterial thrombosis. These tests are the easiest and most affordable to do, making them beneficial in underdeveloped nations. To determine the cut offs of MPV and PDW, which accurately and firmly indicate the possibility of vascular thrombosis, more, larger research are required. This will allow the most suitable, essential interventions to be started as soon as feasible.

Conclusion

According to our research, bigger platelets and higher platelet volume indices are factors in the prothrombotic condition associated with diabetes mellitus. The presence of bigger platelets is likely a risk factor for developing diabetic vascular problems since larger platelets are hemostatically more active.

While doing normal haematological analyses, it is simple to spot bigger platelets since MPV, PDW, and P-LCR are produced as byproducts of automated blood counts. Hence, a helpful predictive predictor of vascular problems in diabetes would be MPV, PDW, and P-LCR.

In order to alert diabetes patients compared to non-diabetics, the obtained cut off values of platelet indices MPV, PDW, and P-LCR were 9.6, 12.2, and 18.4%.

Nevertheless, further research is required to determine if elevated MPV, PDW, and P-LCR are vascular problems' primary or secondary causes. Hence, the platelet volume indices MPV, PDW, and P-LCR offer a significant, easy-to-use, affordable tool that can be helpful in anticipating a thrombotic condition and vascular consequences of diabetes.

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